

REMARKS

Reconsideration of the application is respectfully requested in view of the above amendments and following remarks.

Claims 1-40 were pending in the present application. Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39 were rejected. Claims 3, 4, 10, 12, 13, 18, 25, 32 and 40 were withdrawn from consideration by the Examiner. Claims 1-2 and 5-48 have been canceled. New Claims 49-66 have been added. Currently, Claims 3, 4 and 49-66 are pending in the present application.

In the specification, the new paragraph to be inserted on page 1, line 4, was added after the "TITLE OF THE INVENTION" paragraph on page 1, lines 1-2 and before the "BACKGROUND OF INVENTION" paragraph on page 1, lines 4-12, to provide the priority of the present application.

Applicants have amended the specification to reference the prior filed applications from which the instant application claims benefit. Applicants respectfully contend that the requirements for submitting a petition with such an amendment under 37 C.F.R. §1.78(a)(2)(ii) and (a)(3) have been waived because the U.S. PTO has recognized the claim for benefit on both the Filing Receipt and on the cover page of the related U.S. Patent Application Publication US 2004/0122033 A1 (copies of which are attached). Applicants note that the Notice on Claiming the Benefit of Prior-Filed Applications from Deputy Commissioner Stephan Kunin dated February 24, 2003 specifically states that the requirements under 37 C.F.R. §1.78(a)(3)(ii) and (iii) will be waived if the 'information concerning the claim was recognized by the Office as shown by its inclusion on the filing receipt.'

Claims 1-2 and 5-48 have been canceled without prejudice to filing a divisional application directed to the subject matter claimed therein.

New Claims 49-54 are directed to compositions of two appetite suppressants, a CB-1 antagonist/inverse agonist and phentermine, and methods of using the compositions. Support for the use of a CB-1 antagonist/inverse agonist as an appetite suppressant is found on page 6, line 5 to page 7, line 18, page 8, line 13, and page 41, lines 12-19 of the specification and in original Claim 1 as appetite suppressant (3). Support for the use of phentermine as an appetite suppressant is found on page 9, line 6 of the specification, and in original Claim 1 as appetite suppressant (30).

New Claims 55-59 are directed to compositions of two appetite suppressants, a CB-1 antagonist/inverse agonist and a NPY2 agonist, and methods of using the compositions. Support for the use of a CB-1 antagonist/inverse agonist as an appetite suppressant is found on page 6 line 5 to page 7 line 18, page 8 line 13, and page 41 lines 12-19 of the specification, and in original Claim 1 as appetite suppressant (3). Support for the use of a NPY2 agonist as an appetite suppressant is found on page 8, line 20, and page 42, lines 24-29 of the specification, and in original Claim 1 as appetite suppressant (9).

New Claims 60-66 are directed to compositions of two appetite suppressants, a CB-1 antagonist/inverse agonist and a Mc4r agonist, and methods of using the compositions. Support for the use of a CB-1 antagonist/inverse agonist as an appetite suppressant is found on page 6 line 5 to page 7 line 18, page 8 line 13, and page 41 lines 12-19 of the specification, and in original Claim 1 as appetite suppressant (3). Support for the use of a Mc4r agonist as an appetite suppressant is found on page 8, line 34, and page 43 line 33 to page 44 line 6 of the specification, and in original Claim 1 as appetite suppressant (23).

No new matter has been added to the above-captioned application by the above amendments. Applicants reserve the right to pursue the non-elected subject matter of the claims amended to comply with the restriction requirement in a divisional application.

RESTRICTION REQUIREMENT UNDER 35 U.S.C. 121

The Examiner requested re-affirmation of the elected subject matter when Applicants respond to this Office Action. Applicants have canceled Claims 1-2 and 5-48 of the present invention. Applicants hereby re-affirm the elected subject matter that was elected in the restriction requirements of March 13, 2006 and June 30, 2006 for claims directed to compositions comprising two appetite suppressants: AM-251 and phentermine. New Claims 49-66 are directed to compositions comprised of two appetite suppressants and correspond to a subset of compositions claimed in Claim 1. Applicants request that withdrawn claims 3 and 4, directed to compositions comprising two appetite suppressants, be rejoined if the combination of AM-251 and phentermine is found allowable.

PROVISIONAL REJECTION UNDER JUDICIALLY CREATED DOCTRINE

OF OBVIOUSNESS-TYPE DOUBLE PATENTING

The Examiner stated that Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39, presently Claims 49-66, were provisionally rejected on the ground of non-statutory obviousness type double patenting as

being unpatentable over Claims 1-3, 12, 14-18, 21-26, 34-39, 47-51 and 55 of co-pending application No. 10/520,566 (US 2005/0288213, MacNeil et al.). The Examiner indicated that although the conflicting claims are not identical, they are not patentably distinct because the co-pending application is drawn to the treatment of obesity comprising administering those anti-obesity agents, such as phentermine, beta-3 agonists and CB-1 inverse agonists, that are presently claimed.

Applicants submit that the amended claims of the present application and the claims of Application No. 10/520,566 are patentably distinct.

Applicants submit that there is no overlap between the claims of the present application and Application No. 10/520,566. New Claims 49-66 of the present application, and original Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39 of the present application, do not claim compositions comprising NPY5 antagonists. Withdrawn Claim 12 of the present invention claims a composition comprising a NPY5 antagonist and a 11-beta HSD-1 inhibitor; however, Application No. 10/520566 does not disclose, teach or suggest combinations of NPY5 antagonists and 11-beta HSD-1 inhibitors. Application No. 10/520566 claims compositions of NPY5 antagonists of structural formula I or II and an anti-obesity agent, wherein the definition of anti-obesity agent does not include 11-beta HSD-1 inhibitors. Applicants submit that there is no overlap between either the amended or the original claims of the present invention and the pending claims of Application No. 10/520566. Applicants further submit that the combinations claimed in the present application are novel and are not suggested by Application No. 10/520566. The Examiner has provided no motivation to modify the claims of Application No. 10/520566 to arrive at the presently claimed invention. Therefore a terminal disclaimer is not required. Applicants respectfully request reconsideration and withdrawal of the provisional obviousness type double patenting rejection of Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39, and the allowance of new Claims 49-66.

REJECTION UNDER 35 U.S.C. 112, FIRST PARAGRAPH
FOR LACK OF ENABLEMENT

The Examiner stated that Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39 were rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

The Examiner stated that: 1) the specification provides no support for treating obesity, including overeating and bulimia, comprising administering said combinations; 2) the specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation; 3) the specification fails to provide support for any of the combinations in the treatment of obesity; 4) the claims are very broad with respect to the administration of numerous recited

combinations of active agents; 5) there are no working examples in which any of the recited combinations of anti-obesity agents are administered. Examples 2 and 3 on pages 61-62 of the specification are drawn to the administration of the single agent CB-1 agonist AM-251. The inhibition of food intake is demonstrated in mice models. There is no disclosure drawn to the administration of a combination of agents either through exemplification or in the Figures; 6) Applicants fail to provide guidance as to which particular combination of compounds would be preferred for treating particular types of obesity-related disorders that are encompassed in the claim language. The skilled artisan would expect the interaction of a particular combination of compounds in the treatment of a particular type of obesity to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Applicants respectfully disagree. Applicants submit that rejected Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39, new Claims 49-66, as well as withdrawn Claims 3 and 4, of the present application are described in the specification in such a way as to enable one skilled in the art to practice the invention.

Applicants submit that the specification discloses and provides support for several of the claimed combinations in the treatment of obesity in the Examples and in the Figures. Contrary to the Examiner's assessment, the Figures 1-4 and Examples 1-3 of the instant application provide experimental results that are equivalent to treating obesity using two appetite suppressants that work via two different mechanisms to treat obesity. Figures 1 and 2 show the reduction of food intake and decrease in bodyweight due to the combination of a melanocortin receptor agonist, MT-II, to a Mch1r (melanin concentrating hormone 1 receptor) knock out mouse. A Mch1r knock out mouse is the equivalent of administering a Mch1r antagonist that provides 100% antagonism. Therefore, Figures 1 and 2 show the decrease in food intake and body weight due to the combination of a melanocortin receptor agonist and a Mch1r antagonist, and provide support for the combination of a melanocortin receptor agonist and a Mch1r antagonist to treat obesity. Figure 3 shows the reduction of food intake due to the administration of a CB-1 receptor inverse agonist, AM-251, to a NPY (neuropeptide Y receptor) knock out mouse. A NPY receptor knock out mouse is the equivalent of administering a NPY agonist or antagonist that provides 100% agonism or antagonism of the NPY receptors. Therefore, Figure 4 shows the decrease in food intake due to the combination of a CB-1 receptor inverse agonist and a NPY agonist or antagonist, and provides support for the combination of a CB-1 receptor inverse agonist and a NPY agonist or antagonist to treat obesity. Figure 4 shows the reduction of food intake due to the administration of the CB-1 receptor inverse agonist, AM-251, to a Mch1r (melanin concentrating hormone 1 receptor) knock out mouse. A Mch1r

knock out mouse is the equivalent of administering a Mch1r antagonist that provides 100% antagonism. Therefore, Figure 4 shows the decrease in food intake due to the combination of a CB-1 receptor inverse agonist and a Mch1r antagonist and provides support for the combination of a CB-1 receptor inverse agonist and a Mch1r antagonist to treat obesity. Applicants submit that the specification does provide support for treating obesity comprising administering combinations of two appetite suppressants.

Applicants submit that section 112 does not require working examples (*In re Strahilevitz*, 668, F.2d 1229, 212 U.S.P.Q. 561 (CCPA 1982)) and that the applicants claim scope is not necessarily limited only to those embodiments actually disclosed in the specification (See *Spectra-Physics Inc. v. Coherent Inc.*, 827 F.2d 1524, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987); see also *Utter v. Hiraga*, 845 F.2d 998, 6 U.S.P.Q.2d at 1714 ("A specification may, within the meaning of 3 USC 112, first paragraph, contain a written description of a broadly claimed invention without describing all species that claim encompasses"), and that the embodiment need not necessarily have even been reduced to practice (See *In re Wright*, 999 F.2d 1557; 1561, 27 U.S.P.Q.2d 1510, 1513).

Applicants further submit that the inhibition of food intake is demonstrated in mice models, and that although the claimed invention has not yet been tested in human clinical trials for safety and effectiveness, such trials are not required to establish utility under the patent law:

Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating the incentive to pursue, through research and development, potential cures in many crucial areas...

In re Brana, 34 U.S. P.Q.2d 1436, 1442-3 (Fed Cir. 1995)

Finally, the Applicants submit that the specification provides guidance that would allow the skilled artisan to practice the instant invention without undue experimentation. The claims recite combinations of anti-obesity agents that work by different biological mechanisms and whose combination will result in a decrease in food intake and body weight. One of ordinary skill in the art can readily identify anti-obesity agents, such as appetite suppressants, useful in the compositions and methods of the present invention. As disclosed on page 40 line 28 to page 41 line 7, one of ordinary skill in the art can readily determine if a compound works as an appetite suppressant by evaluating the compound in rodents according to the procedures described in the art. One of skill in the art can also determine if the anti-

obesity agent works by a particular biological mechanism of action with routine receptor binding studies and functional activity assays known in the art. Based on the determination of the mechanism of action of a particular appetite suppressant, a skilled artisan can determine which other appetite suppressant with a known biological mechanism of action would work in combination with the first appetite suppressant. The court has held that "[A] considerable amount of experimentation is permissible, if it is merely routine, or is the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (*In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404 (quoting *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982)). Applicants submit that the specification provides guidance as to which compounds can be combined based on their mechanisms of action, and provides guidance with respect to the direction in which experimentation should proceed by disclosing which types of appetite suppressants may be combined based on their particular mechanisms of action. Compositions comprising two appetite suppressants can be evaluated in rodents according to the procedures described in: Daniels, A.J. et. al., *Regulatory Peptides*, 106:47-54 (2002); Halaas, J.L. et. al., *Science*, 269: 543-546 (1995), and Strack, A.M., *Obesity Research*, 10:173-81 (2002) as disclosed on page 40, lines 28-32 of the specification.

In view of the above arguments, Applicants respectfully submits that the present Claims are adequately enabled and request reconsideration and withdrawal of the rejection of Claims 1, 2, 5-9, 11, 14-17, 19-24, 26-31 and 33-39 under 35 USC 112, first paragraph. Furthermore, Applicants request that Claims 3 and 4 be rejoined and allowed and that new Claims 49-66 be allowed.

Applicants believe that all of the rejections have been overcome and therefore earnestly solicit an early Notice of Allowance.

Respectfully submitted,

By



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(54) **COMBINATION THERAPY FOR THE
TREATMENT OF OBESITY**

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(57) **ABSTRACT**

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The present invention relates to compositions comprising an appetite suppressant and/or a metabolic rate enhancer and/or a nutrient absorption inhibitor useful for the treatment of obesity, and obesity-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compositions, medicaments, and kits useful in carrying out these methods.

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Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

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